which comprises the step of expressing the set of DNA sequences within a producer cell according to claim 54 within the subject.

59. (NEW) A method for making a producer cell *in vivo* in a subject which producer cell is capable of producing a replication defective retroviral vector in an infective retroviral particle, which comprises the step of introducing a set of DNA sequences comprising
a first DNA sequence encoding replication defective retroviral vector, which comprises

(i) a defective retroviral genome lacking functional env and functional *gag-pol* genes but having the remaining components essential for retroviral function; and

(ii) at least one heterologous gene; and

a second DNA sequence encoding a DNA sequence capable of encoding packaging components env and *gag-pol* wherein the DNA sequence encoding env is present on a separate construct to the DNA sequence encoding *gag-pol* into a cell within a subject causing conversion into the cell into a producer cell.

60. (NEW) A method or cell according to claim 1, wherein the heterologous gene comprises at least one therapeutically active gene.

61. (NEW) A method or cell according to claim 1, wherein the components essential for retroviral function are any one or more of a primer binding site, integration sites and a packaging signal.

62. (NEW) A method of performing gene therapy on a subject, which comprises the step of introducing a therapeutically active gene into a target cell in a subject by a method according to claim 1.

REMARKS

Priority

The priority claim was objected to for failure to make specific reference to the prior applications to which priority is claimed in the first sentence of the specification. Applicants respectfully submit that the amendments to the specification overcome this objection.

Abstract

The language and format of the abstract was objected to as containing legal phraseology and for missing pronouns. Applicants respectfully submit that the new Abstract overcomes this objection.

Rejections under 35 U.S.C. § 101

Claim 41 was rejected under 35 U.S.C. § 101 as reciting a use, without setting forth any process steps. Claim 41 has been canceled without prejudice. Therefore this rejection is now moot.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 22-25, 31-34 and 42-45 were rejected under 35 U.S.C. § 112, first paragraph, as not enabled. Claims 22-25, 31-34 and 42-45 have been canceled without prejudice. Therefore this rejection is now moot. Applicants respectfully traverse this rejection as it may be applied to any of the pending claims.

Applicants respectfully submit that the application provides sufficient exemplification to make and use the invention as claimed. The examples provide the skilled person with a number of delivery methods and producer systems. Applicants are not required to provide examples of all permutations of delivery methods/heterologous genes/producer cells/diseases.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. A patent may be enabling even though some experimentation is necessary, so long as the amount of experimentation is not "undue". See *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991); and *United States v. Telectronics, Inc.* 857 F.2d 778 (Fed. Cir. 1988).

As is clear from the present application (page 1, line 25-33), previously known approaches for gene delivery were associated with a number of drawbacks. For example, methods of non-viral delivery have the problem that DNA is confined to the initial target cells and is short-lived, necessitating repeated treatments with the DNA. Retrovirus-mediated gene delivery in vivo is commonly inefficient because there is no extended exposure of the cells to viral particles. The prior art cited by the examiner merely reinforces this point.

Despite the overall prejudice in the art, the present invention addresses the problem of low efficiency of gene delivery using known techniques, and provides a solution. In the method of the present invention, a combination of DNA sequences known as a vector production system (VPS) is used to create an *in situ* retroviral factory (ISRF), which is a retroviral producer cell created from one of the subject's own cells. The ISRF produces retroviral particles, which transduce neighboring target cells. This system has a number of advantages (see the present application page 9, line 5-page 11 line 4). In particular the system represents an improvement over conventional retrovirus-mediated *in vivo* gene delivery because:

(a) a much higher local concentration of retroviral particles is achieved, because the particles are produced *in situ*;

(b) the target cells are exposed to retroviral vectors for a considerably extended period because the ISRF produces retroviral particles, which are released from the cell for as long as the VPS persists, which may be of the order of weeks to months, or even years.

Applicants respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 22, 25, 31, 33-34 and 41-46 were rejected under 35 U.S.C. § 112, second paragraph as indefinite. Claims 22, 25, 31, 33-34 and 41-46 have been canceled. Therefore, this rejection is now moot. Applicants respectfully traverse this rejection as it may be applied to any of the remaining claims.

In the amended claims, the phrase "the cell" refers to a cell before conversion to a producer cell. Producer cells and target cells are referred to in full to avoid confusion. "The patient" has been deleted. The claims now recite a "subject" throughout. The terms "suitable" and "contain" have been removed.

The claim relating to gene therapy (new claim 62) sets forth a step involved in the process.

With respect to the following phrases: "expressing within a producer cell"; "essential for retroviral functions"; "introducing"; and "capable of", Applicants respectfully submit that their meaning is clear and distinct to one skilled in the art.

Rejections under 35 U.S.C. § 102

Claims 31-34 were rejected under 35 U.S.C. § 102(a) as anticipated by *Garver*. Claims 31-34 have been canceled. Therefore this rejection is now moot. Applicants respectfully traverse this rejection as it may be applied to any of the remaining claims.

The amended claims specify that the DNA sequence encoding *env* is present on a separate construct than the DNA sequence encoding *gag-pol*. *Garver et al.* does not teach or suggest a system that includes a second "complementing" nucleic acid construct. We submit therefore that the subject matter of the claims in novel and inventive over the cited prior art. Applicants therefore request withdrawal of this rejection.

CONCLUSION

In view of the amendments and remarks presented herein, it is respectfully submitted that the application is in condition for allowance and notification to that effect is earnestly solicited. The Examiner is encouraged to contact Applicant's undersigned attorney to discuss this application if any questions should arise upon further examination of the pending claims.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

Dated: Sept. 27, 2006

By _____
Melissa Jean Pytel
Reg. No. 41,512